

Supplementary Information

An international multicenter study of MASLD prevalence among children and adolescents assessed by VCTE

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Supplementary Methods

Study design and population

Data were collected from participating centers using predefined inclusion and exclusion criteria and a standardized data collection form completed by each participating center. Eligible participants were children and adolescents aged 18 years or younger with available VCTE examination data. Exclusion criteria included having other chronic liver diseases, such as viral hepatitis, HIV infection, excessive alcohol consumption (> 30 g/day for males and > 20 g/day for females), or a history of any tumors. Initially, 9804 participants from multiple research centers were enrolled, and data were collected until August 2024 (Because the data from Africa were available only from Egypt and the sample size was small, Africa was not included). Participants were excluded if they were older than 18 years ($n = 13$), had missing VCTE results ($n = 94$), had missing or incorrect age data ($n = 12$), had fewer than 10 valid readings for controlled attenuation parameter (CAP) scores ($n = 29$), or had an interquartile range (IQR) of median liver stiffness measurement (LSM) values exceeding 30% ($n = 36$).

Children under 6 years of age were excluded because participants in this age group were recruited only from community-based populations in China, and the sample size was limited ($n = 268$; median age, 4.75 years). In this population, the estimated prevalence of MASLD; S1, S2, and S3 steatosis; and F1, F2, and $\geq$ F3 fibrosis were 4.48% (95% CI: 2.33–7.69), 7.46% (95% CI: 4.62–11.29), 3.36% (95% CI: 1.55–6.28), 1.49% (95% CI: 0.41–3.78), 19.78% (95% CI: 15.18–25.06), 2.61% (95% CI: 1.06–5.31), and 0.00%, respectively.

Vibration-controlled transient elastography and MASLD definition

All operators were blinded to both the diagnosis and clinical data, and had completed more than 100 VCTE examinations before the study began. All participants were asked to fast for at least 4 hours or overnight before the VCTE assessment. The VCTE examination was deemed successful when at least 10 valid measurements were obtained, the success rate was $\geq 60\%$, and the IQR was $\leq 30\%$ of the LSM value. Probe selection followed the manufacturer's instructions. The S probe was used for participants with a thoracic circumference < 75 cm, whereas the M probe was used initially for participants with a thoracic circumference ≥ 75 cm. When the device indicated the XL probe should be used, the XL probe was selected accordingly. Participants with unsuccessful examinations were excluded from the analysis. Steatosis was evaluated based on the median CAP score in decibels per meter (dB/m), while fibrosis was assessed using the median LSM in kilopascals (kPa). Hepatic steatosis was graded according to an individual patient data meta-analysis,¹ which established the following cut-off values: S0 as a score below 248 dB/m; S1 as a score ranging from 248 to less than 268 dB/m (mild); S2

as a score ranging from 268 to less than 280 dB/m (moderate); and S3 as a score of 280 dB/m or higher (severe). CAP scores of 248 dB/m or greater ($\geq$ S1) indicated suspected steatosis. Liver fibrosis was graded using the following thresholds:² F0 as a score of less than 5.1 kPa; F1 as a score of 5.1 to less than 7.4 kPa (any fibrosis); F2 as a score of 7.4 to less than 10.2 kPa (significant fibrosis); and $\geq$ F3 as a score of 10.2 kPa or more (advanced fibrosis and above, including F3 and F4 fibrosis), based on previous studies^{3,4} that showed good diagnostic performance compared with liver biopsy.

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Supplementary Table 1. Characteristics of participants between case and control groups.

	Non-MASLD	MASLD	<i>P</i>
N	6177	2970	
Age (years)	10.0 (7.5, 13.3)	15.0 (12.3, 16.8)	< 0.001
6–11	4047 (65.5)	697 (23.5)	< 0.001
12–18	2130 (34.5)	2273 (76.5)	
Sex			
Male	3378 (54.7)	2001 (67.4)	< 0.001
Female	2799 (45.3)	969 (32.6)	
Ethnicity			
Non-Hispanic White	465 (7.5)	204 (6.9)	< 0.001
Non-Hispanic Black	322 (5.2)	77 (2.6)	
Hispanic	180 (2.9)	203 (6.8)	
Asian	4933 (79.9)	2351 (79.2)	
Others	277 (4.5)	135 (4.5)	
Population source			
Community	4766 (77.2)	1018 (34.3)	< 0.001
Hospital	1411 (22.8)	1952 (65.7)	
LSM (kPa)	4.20 (3.50, 5.10)	5.80 (4.70, 7.60)	< 0.001
< 5.1	4565 (73.9)	994 (33.5)	< 0.001
5.1–7.4	1407 (22.8)	1177 (39.6)	
7.4–10.2	137 (2.2)	517 (17.4)	
≥ 10.2	68 (1.1)	282 (9.5)	
CAP (dB/m)	194 (169, 219)	305 (276, 335)	< 0.001
< 248	6023 (97.5)	0 (0.0)	< 0.001
248–268	83 (1.3)	536 (18.0)	
268–280	34 (0.6)	309 (10.4)	
≥ 280	37 (0.6)	2125 (71.5)	
Weight status/BMI z-score	0.56 (–0.35, 1.57)	2.46 (1.99, 2.94)	< 0.001
Normal weight or below	3805 (61.6)	75 (2.5)	< 0.001
Overweight	1400 (22.7)	684 (23.0)	
Obesity	972 (15.7)	2211 (74.4)	
Blood pressure [†]			
Normal	3234 (89.4)	1590 (84.5)	< 0.001
Elevated	385 (10.6)	292 (15.5)	
Glucose (mmol/L)	4.96 (4.70, 5.20)	5.16 (4.86, 5.50)	< 0.001
Normal	5585 (90.4)	2269 (76.4)	
Elevated	592 (9.6)	701 (23.6)	
ALT (IU/L)	14.00 (11.30, 18.00)	33.00 (20.00, 59.00)	< 0.001
Normal	5423 (87.8)	1055 (35.5)	
Elevated	754 (12.2)	1915 (64.5)	
AST (IU/L)	25.00 (20.40, 29.60)	28.80 (21.00, 46.00)	< 0.001
Normal	5489 (88.9)	1850 (62.3)	
Elevated	688 (11.1)	1120 (37.7)	
GGT (IU/L)	13.24 (11.40, 16.56)	29.00 (19.00, 54.00)	< 0.001
Platelet count (*10 ⁹ /L)	292 (253, 329)	293 (260, 329)	0.030
Total cholesterol (mmol/L)	4.46 (3.99, 4.88)	4.45 (3.96, 4.99)	0.095

HDL cholesterol (mmol/L)	1.49 (1.29, 1.68)	1.19 (1.03, 1.36)	< 0.001
Triglycerides (mmol/L) [†]	0.72 (0.56, 0.97)	1.31 (0.95, 1.89)	< 0.001
LDL cholesterol (mmol/L) [†]	2.35 (1.97, 2.81)	2.67 (2.17, 3.20)	< 0.001

Variables are presented as median (IQR) or n (%). [†] Missing data on blood pressure (n = 5990), triglycerides (n = 3625), and LDL cholesterol (n = 3880). [‡] Elevated blood pressure was defined as SBP $\geq$ 120 mm Hg, or DBP $\geq$ 80 mm Hg for individuals aged <13 years, and DBP $\geq$ 85 mm Hg for those aged $\geq$ 13 years; elevated glucose was defined as fasting serum glucose $\geq$ 5.6 mmol/L; elevated ALT was identified as ALT >22 IU/L for female participants and >26 IU/L for male participants; elevated AST was identified as AST >35 U/L; BMI z-scores were calculated as continuous variables.

P values are reported as two-sided Pearson's chi-squared tests for categorical variables and two-sided Wilcoxon rank-sum tests for continuous variables. Exact test statistics and available exact *P* values are provided in Source data.

LSM, liver stiffness measurement; CAP, controlled attenuation parameter; BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MASLD, metabolic dysfunction-associated steatotic liver disease.

Supplementary Table 2. Characteristics of participants included in the study across continents.

Items	All participants for continents			Community population for continents			Hospital population for continents	
	North America	South America	Asia	North America	South America	Asia	North America	Asia
Age (year)	15.0 (13.0, 16.4)	16.1 (15.1, 16.8)	10.5 (8.0, 14.3)	15.0 (13.0, 17.0)	16.1 (15.1, 16.8)	8.8 (7.1, 11.4)	12.0 (10.5, 14.7)	13.5 (10.2, 16.3)
6-11	337 (18.5)	0 (0.0)	4429 (60.9)	227 (14.1)	0 (0.0)	3189 (78.1)	110 (51.2)	1240 (38.9)
12-18	1484 (81.5)	96 (100.0)	2841 (39.1)	1379 (85.9)	96 (100.0)	894 (21.9)	105 (48.8)	1947 (61.1)
Weight status/BMI z-score	1.26 (0.20, 2.33)	1.91 (0.88, 2.59)	1.41 (0.03, 2.34)	1.04 (0.09, 2.12)	1.91 (0.88, 2.59)	0.69 (-0.28, 1.71)	2.53 (2.09, 2.96)	2.17 (1.21, 2.74)
Normal weight or below	804 (44.2)	27 (28.1)	3055 (42.0)	788 (49.1)	27 (28.1)	2326 (57.0)	16 (7.4)	729 (22.9)
Overweight	400 (22.0)	25 (26.0)	1665 (22.9)	372 (23.2)	25 (26.0)	1006 (24.6)	28 (13.0)	659 (20.7)
Obesity	617 (33.9)	44 (45.8)	2550 (35.1)	446 (27.8)	44 (45.8)	751 (18.4)	171 (79.5)	1799 (56.4)
Sex								
Male	977 (53.7)	41 (42.7)	4391 (60.4)	858 (53.4)	41 (42.7)	2376 (58.2)	119 (55.3)	2015 (63.2)
Female	844 (46.3)	55 (57.3)	2879 (39.6)	748 (46.6)	55 (57.3)	1707 (41.8)	96 (44.7)	1172 (36.8)

Variables are presented as medians (IQR) or n (%).

Supplementary Table 3. Composition of the study groups participating in the study.

Center	Country	Continent	Sample size	Ethics approval number
Affiliated Children's Hospital of Jiangnan University	China	Asia	3496	WXCH2024-02-062
The First Affiliated Hospital of Wenzhou Medical University	China	Asia	212	KY2023-120
Storr Liver Centre	Australia	Oceania	8	2019/ETH02319
The First Affiliated Hospital of Ningbo University	China	Asia	416	2021-R168
Yonsei University College of Medicine	Korea	Asia	512	YUHS 4-2024-1643
McGill University Health Centre	Canada	North America	74	MP-37-2021-6461
National Autonomous University of Mexico	Mexico	North America	100	2024-EXT-820
National Health and Nutrition Examination Survey (NHANES) database	USA	North America	1585	2011-17 and 2018-01
Xiamen Hospital of Traditional Chinese Medicine	China	Asia	18	2019-J10-18
The First Affiliated Hospital, Sun Yat-sen University	China	Asia	25	2020-187
Guangdong Provincial Hospital of Traditional Chinese Medicine	China	Asia	113	BF2024-025-01
The First Affiliated Hospital, Fujian Medical University	China	Asia	85	2024-375
Bambino Gesù' Children Hospital	Italy	Europe	111	3075_OPBG_2023
General Hospital of Mexico	Mexico	North America	77	DI/17/311/03/028
The Second People's Hospital of Tianjin	China	Asia	76	2012-002-1
King Chulalongkorn Memorial Hospital	Thailand	Asia	54	526/62
National University Hospital	Singapore	Asia	15	NUH-RNR-2024-0029
Hangzhou Normal University Affiliated Hospital	China	Asia	135	2023(E2)-HS-091
Xinhua Hospital, Shanghai Jiao Tong University School of Medicine	China	Asia	851	XHEC-C-2013-001-2
Liaocheng People's Hospital	China	Asia	107	2023033
National and Kapodistrian University	Greece	Europe	27	29661/23-12-16
Qilu Hospital, Shandong University	China	Asia	260	KYLL-202301-008-1
The First Affiliated Hospital of Nanjing Medical University	China	Asia	26	2021-SR-344
Sheikh Khalifa Medical City	United Arab Emirates	Asia	12	REC-04.06.2024 [RS-878]
Recep Tayyip Erdoğan University	Turkey	Asia	88	2024/180
Salmaniya Medical Complex	Bahrain	Asia	5	28-220224/St2
Faculty of Medicine, University "Titu Maiorescu"	Romania	Europe	4	REC38761-2020
University of Bologna	Italy	Europe	23	252/2024/Sper/AOUBo
Universidade Federal do Rio de Janeiro	Brazil	South America	26	CAAE 45572715.8.1001.5286
Nanjing Hospital of Chinese Medicine	China	Asia	136	KY2022294
Pontificia Universidad Católica de Chile	Chile	South America	70	190528006
Shuguang Hospital affiliated to Shanghai University of Traditional Chinese Medicine	China	Asia	39	2023-1415-182-01
The Affiliated Hospital of Nanjing University of Chinese Medicine	China	Asia	717	2022NL-122-01
Faculty of Medicine, University Malaya	Malaysia	Asia	5	202069-8734
The Second Affiliated Hospital of Wenzhou Medical University	China	Asia	87	LCKY2018-20
West China Hospital of Sichuan University	China	Asia	182	2025-831
The Sixth People's Hospital of ChengDu	China	Asia	15	2020-L-004
Shanghai Fifth People's Hospital	China	Asia	12	2022-EC-121X1

Supplementary Table 4. Proportions of missing values and distribution of each variable before and after imputation.

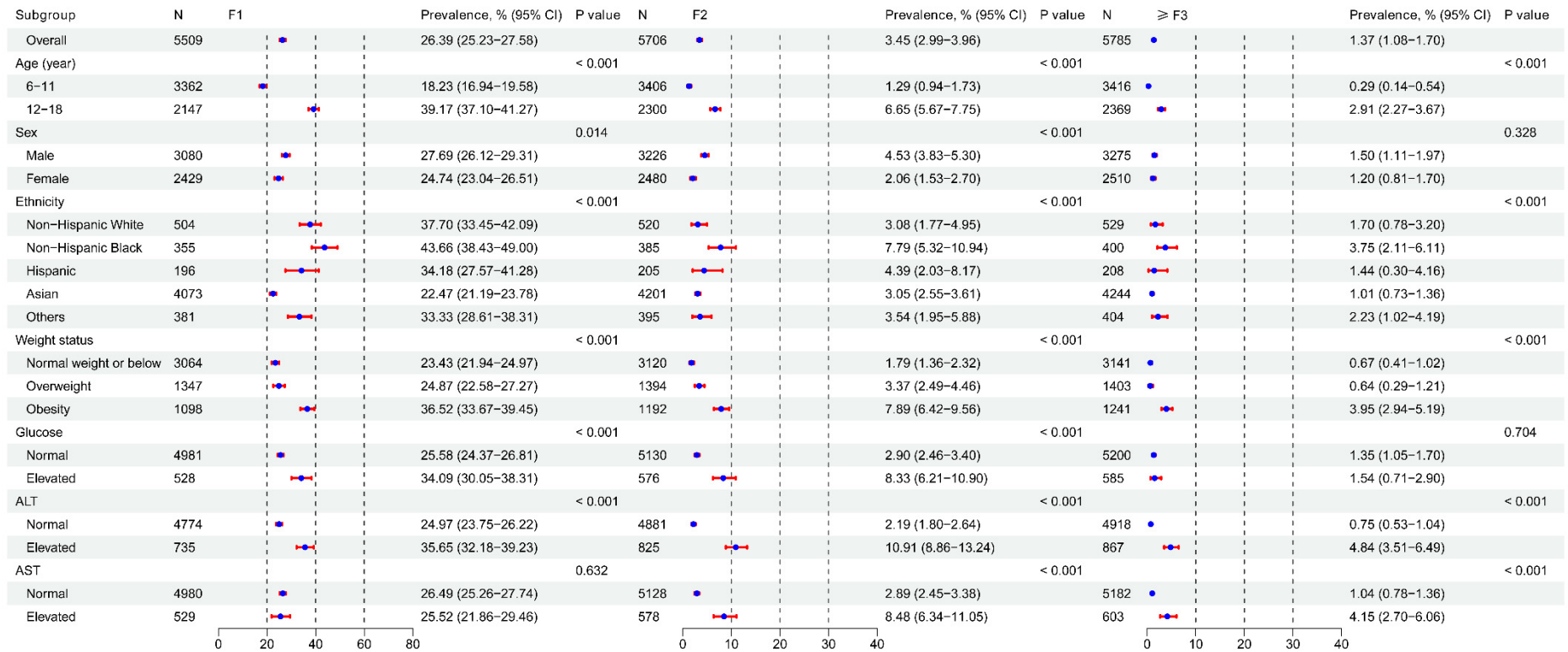
Variables	Missing values (n, %)	Before imputation		After imputation	
		Mean $\pm$ SD	Median (25th, 75th)	Mean $\pm$ SD	Median (25th, 75th)
Height (cm)	688 (7.3%)	150.01 $\pm$ 19.00	152.00 (133.00, 165.60)	151.17 $\pm$ 18.97	154.20 (134.00, 167.00)
Weight (kg)	679 (7.2%)	53.42 $\pm$ 26.59	48.50 (30.80, 70.90)	55.44 $\pm$ 27.05	51.08 (32.00, 75.00)
Glucose (mmol/L)	3034 (32.4%)	5.14 $\pm$ 1.24	5.00 (4.70, 5.30)	5.13 $\pm$ 1.06	5.00 (4.72, 5.30)
ALT (IU/L)	2056 (21.9%)	30.07 $\pm$ 42.02	16.20 (12.00, 29.00)	28.82 $\pm$ 38.20	16.50 (12.36, 29.00)
AST (IU/L)	2616 (27.9%)	32.60 $\pm$ 33.84	24.00 (19.00, 31.00)	32.25 $\pm$ 29.51	25.40 (20.60, 32.40)
GGT (IU/L)	2827 (30.2%)	26.99 $\pm$ 33.82	15.00 (12.00, 25.00)	25.58 $\pm$ 30.04	15.00 (12.00, 24.70)
Platelet count (*10 ⁹ /L)	2671 (28.5%)	292.10 $\pm$ 70.70	287.00 (245.00, 333.00)	294.28 $\pm$ 62.80	292.00 (255.00, 329.00)
Total cholesterol (mmol/L)	3088 (33.0%)	4.43 $\pm$ 0.94	4.37 (3.81, 4.97)	4.47 $\pm$ 0.82	4.45 (3.98, 4.91)
HDL cholesterol (mmol/L)	3221 (34.4%)	1.39 $\pm$ 0.40	1.34 (1.13, 1.59)	1.41 $\pm$ 0.36	1.39 (1.17, 1.60)
Blood pressure [†]	3647 (38.9%)	-	-	-	-
Triglycerides (mmol/L) [†]	3648 (39.0%)	-	-	-	-
LDL cholesterol (mmol/L) [†]	3917 (41.8%)	-	-	-	-
Year of the examination [‡]	114 (1.2%)	-	-	-	-
CAP/MASLD [‡]	205 (2.1%)	-	-	-	-

[†] Variables with excessively high proportions of missing data were excluded from imputation; [‡]Categorical variables and the primary outcome were considered not suitable for imputation.

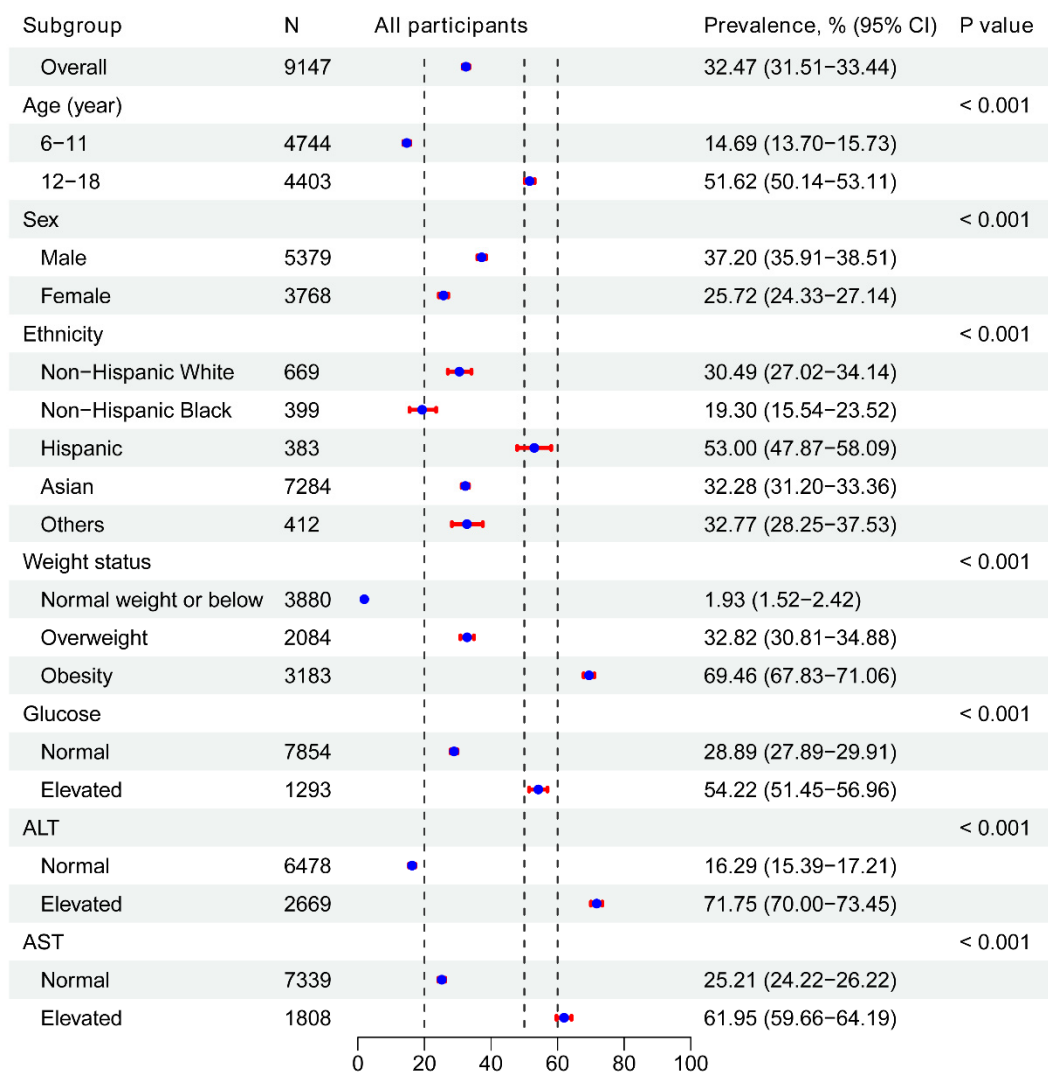
Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; CAP, controlled attenuation parameter; MASLD, metabolic dysfunction-associated steatotic liver disease.



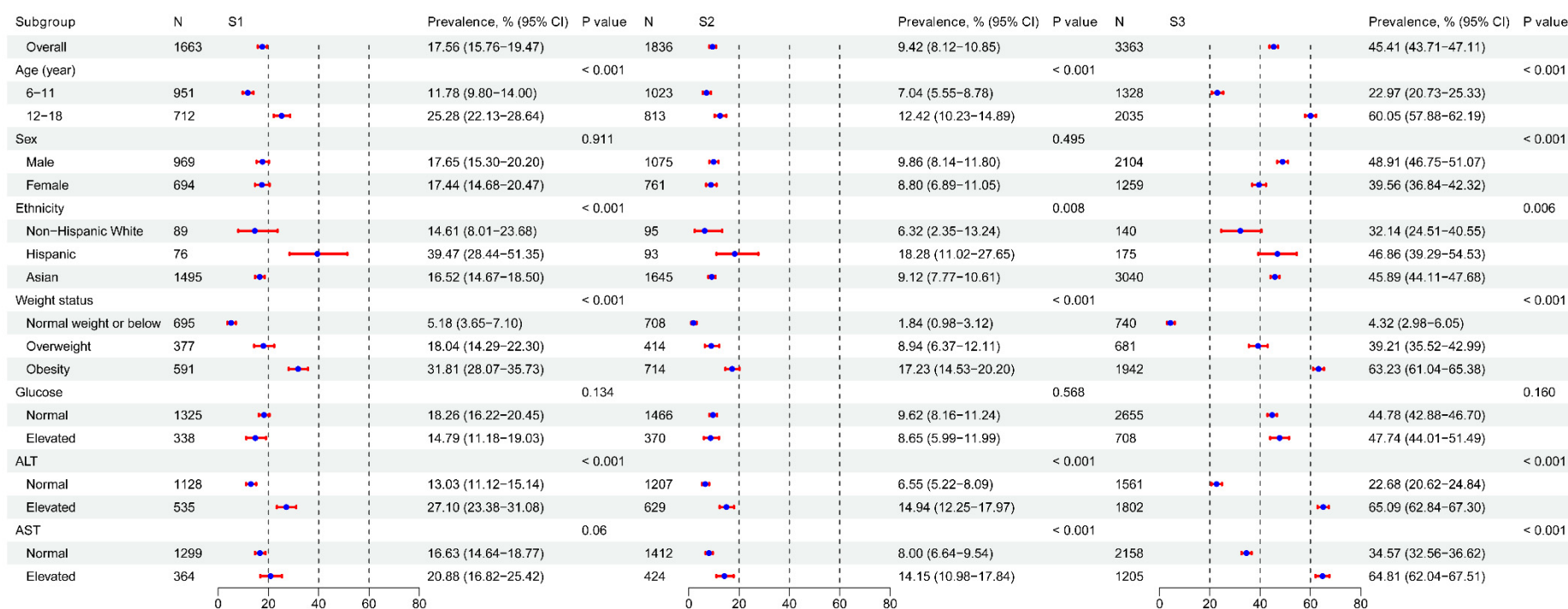
Supplementary Fig. 1. Prevalence of hepatic steatosis grades in the overall population and subgroups of the community-based population. Blue dots represent subgroup-specific prevalence estimates for S1, S2 and S3, and red horizontal lines indicate the corresponding 95% confidence intervals. Sample sizes used to derive each estimate are shown in the corresponding N columns. Prevalence estimates are presented as percentages (95% confidence intervals). P values were calculated using two-sided Pearson's chi-squared tests to compare the prevalence of each hepatic steatosis grade across categories within each subgroup. Exact P values and associated test statistics are provided in the Source data. ALT, alanine aminotransferase; AST, aspartate aminotransferase.



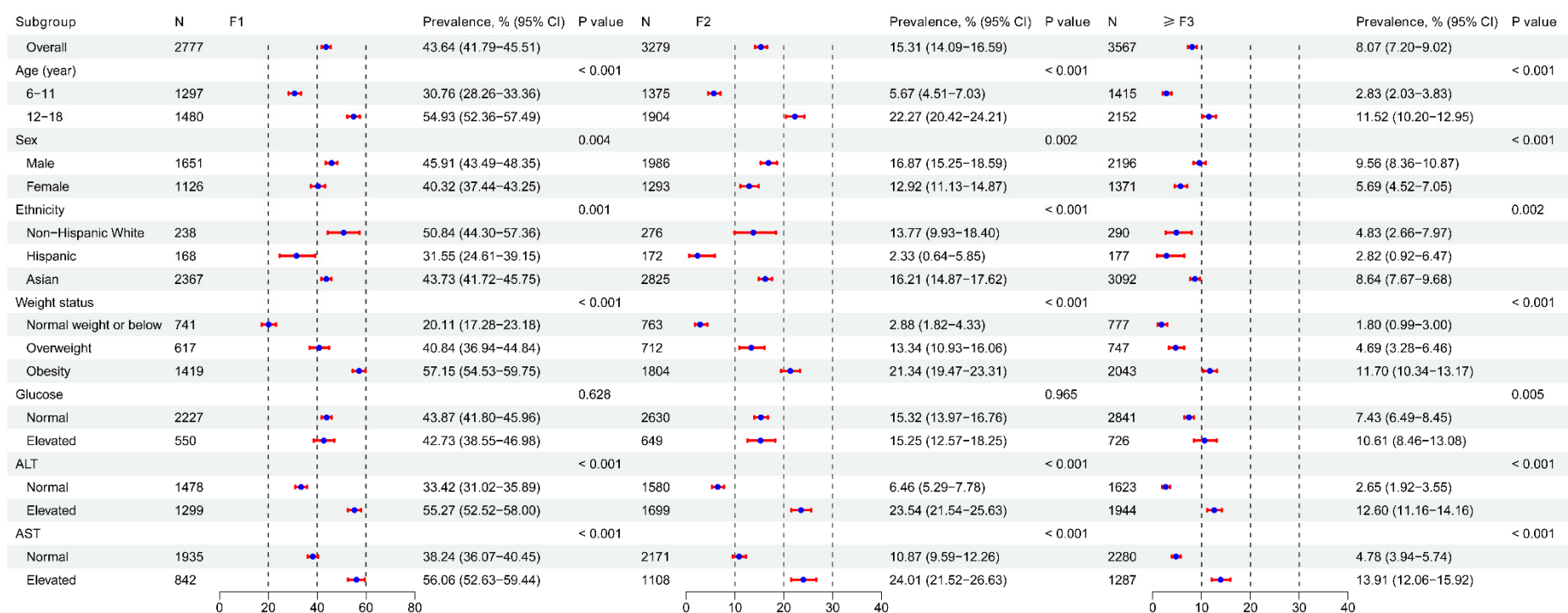
Supplementary Fig. 2. Prevalence of liver fibrosis grades in the overall population and subgroups of the community-based population. Blue dots represent subgroup-specific prevalence estimates for F1, F2 and $\geq$ F3, and red horizontal lines indicate the corresponding 95% confidence intervals. Sample sizes used to derive each estimate are shown in the corresponding N columns. Prevalence estimates are presented as percentages (95% confidence intervals). *P* values were calculated using two-sided Pearson's chi-squared tests to compare the prevalence of each liver fibrosis grade across categories within each subgroup. Exact *P* values and associated test statistics are provided in the Source data. ALT, alanine aminotransferase; AST, aspartate aminotransferase.



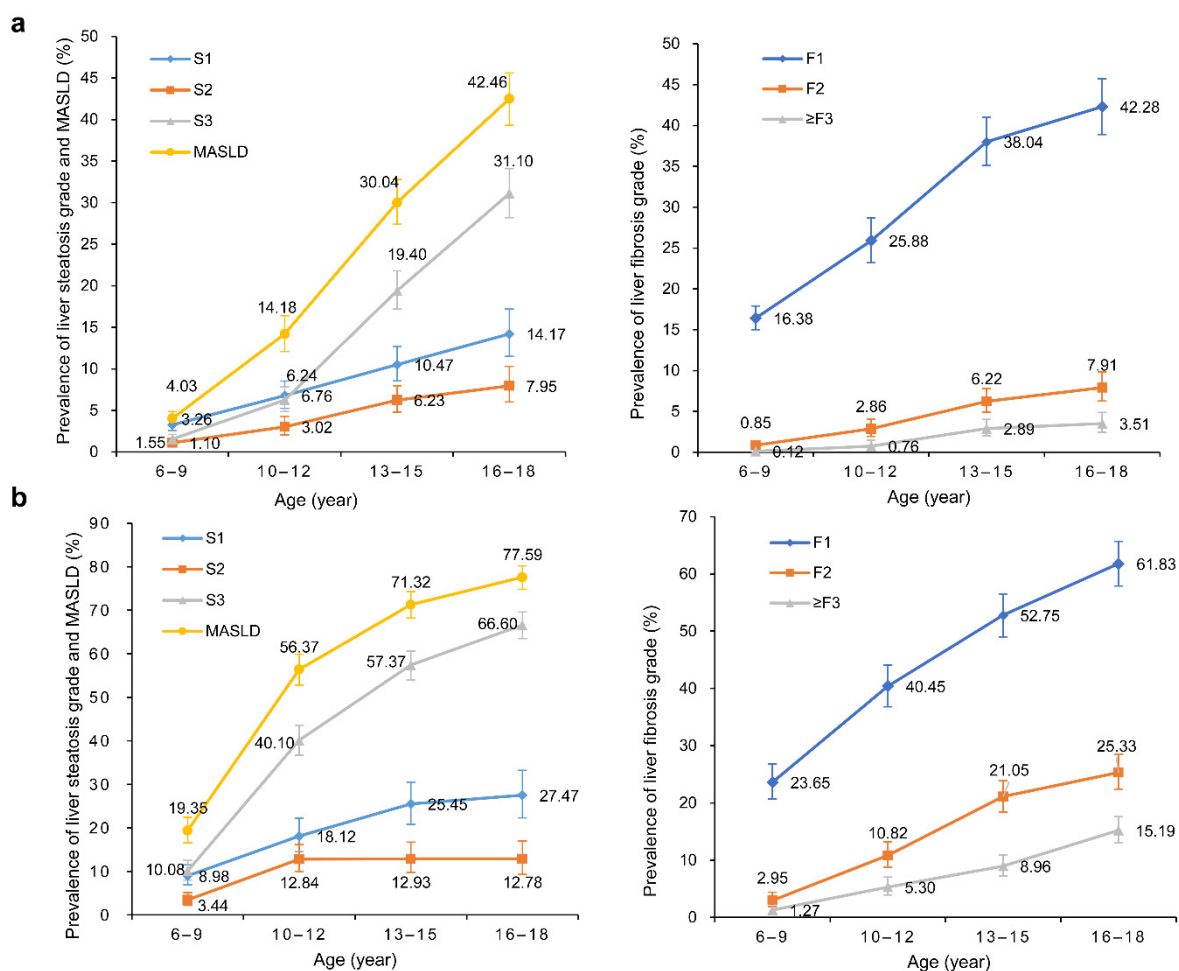
Supplementary Fig. 3. Prevalence of MASLD in the overall population and subgroups. Blue dots represent subgroup-specific MASLD prevalence estimates, and red horizontal lines indicate the corresponding 95% confidence intervals. Sample sizes used to derive each estimate are shown in the corresponding N column. Prevalence estimates are presented as percentages (95% confidence intervals). *P* values were calculated using two-sided Pearson's chi-squared tests to compare MASLD prevalence across categories within each subgroup; exact *P* values and associated test statistics are provided in the Source data. ALT, alanine aminotransferase; AST, aspartate aminotransferase.



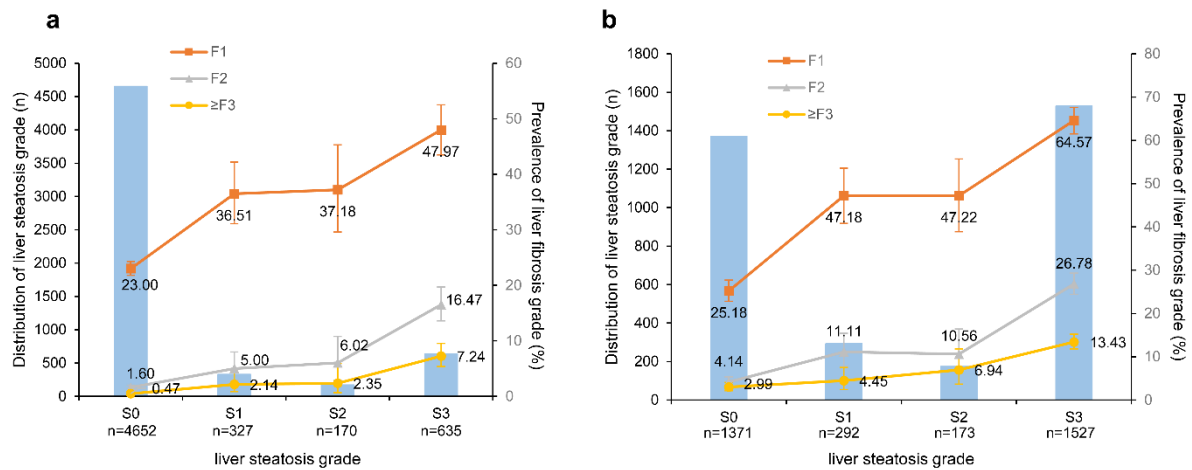
Supplementary Fig. 4. Prevalence of hepatic steatosis grades in the overall population and subgroups of the hospital-based population. Blue dots represent subgroup-specific prevalence estimates for S1, S2 and S3, and red horizontal lines indicate the corresponding 95% confidence intervals. Sample sizes used to derive each estimate are shown in the corresponding N columns. Prevalence estimates are presented as percentages (95% confidence intervals). P values were calculated using two-sided Pearson's chi-squared tests to compare the prevalence of each hepatic steatosis grade across categories within each subgroup. Exact P values and associated test statistics are provided in the Source data. ALT, alanine aminotransferase; AST, aspartate aminotransferase.



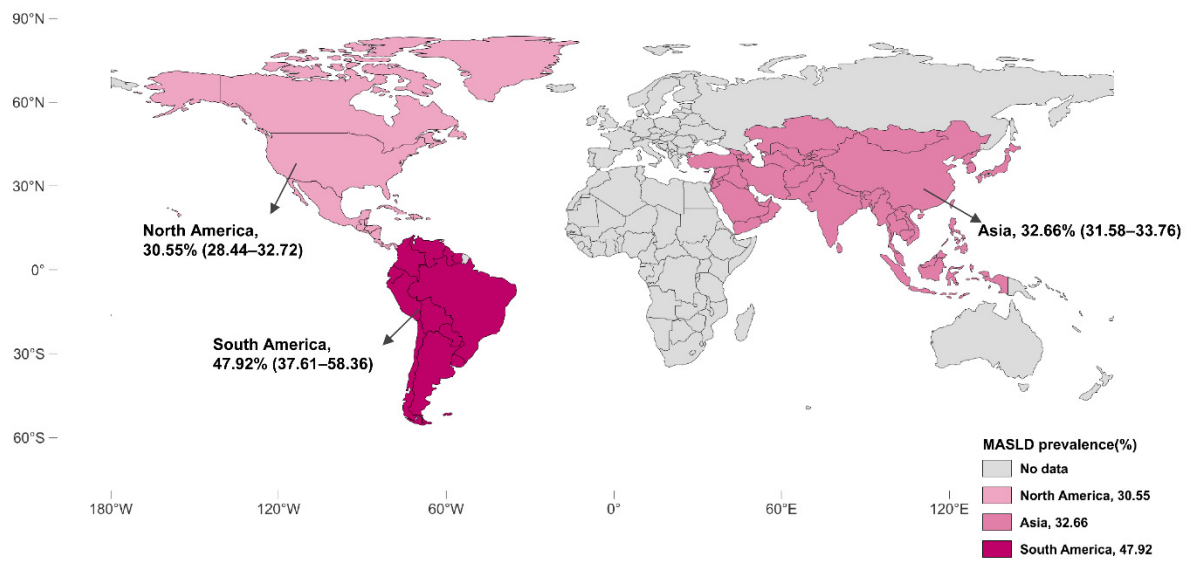
Supplementary Fig. 5. Prevalence of liver fibrosis grades in the overall population and subgroups of hospital-based population. Blue dots represent subgroup-specific prevalence estimates for F1, F2 and $\geq$ F3, and red horizontal lines indicate the corresponding 95% confidence intervals. Sample sizes used to derive each estimate are shown in the corresponding N columns. Prevalence estimates are presented as percentages (95% confidence intervals). *P* values were calculated using two-sided Pearson's chi-squared tests to compare the prevalence of each liver fibrosis grade across categories within each subgroup. Exact *P* values and associated test statistics are provided in the Source data. ALT, alanine aminotransferase; AST, aspartate aminotransferase.



Supplementary Fig. 6. Prevalence of MASLD, liver steatosis, and liver fibrosis based on age groups. a, community-based population; **b,** hospital-based population. In each panel, the left plot shows the prevalence of steatosis grades S1–S3 and MASLD, and the right plot shows the prevalence of fibrosis grades F1, F2 and $\geq$ F3 across age groups. Points represent age-specific prevalence estimates, and error bars indicate 95% confidence intervals. Lines connect estimates across independent age groups for visual comparison. Prevalence estimates are presented as percentages. Sample sizes vary by age group and outcome category; the exact sample size used for each estimate is provided in the Source data. S1–S3, steatosis grades 1–3; F1–F3, fibrosis grades 1–3; MASLD, metabolic dysfunction-associated steatotic liver disease.



Supplementary Fig. 7. Prevalence of liver fibrosis stages among participants with different hepatic steatosis grades. **a**, community-based population; **b**, hospital-based population. Blue bars indicate the total number of participants in each liver steatosis grade (S0–S3) and are interpreted using the left y axis. Lines indicate the prevalence of liver fibrosis stages F1, F2 and $\geq$ F3 within each steatosis-grade category and are interpreted using the right y axis. Points represent prevalence estimates, and error bars indicate 95% confidence intervals. The sample sizes shown below each steatosis-grade category correspond to the total number of participants represented by the blue bars. As the denominators used to calculate the prevalence estimates for individual fibrosis stages may vary, the exact sample size for each estimate is provided in the Source data. Prevalence estimates are presented as percentages. S0–S3, steatosis grades 0–3; F1–F3, fibrosis grades 1–3.



Supplementary Fig. 8. Prevalence estimates of MASLD in the overall population, categorized by continent. Prevalence estimates are presented as percentages with 95% confidence intervals. Sample sizes for participants in North America, South America and Asia were $n = 1821$, 96 and 7270 , respectively. Base map data were obtained from Natural Earth (public-domain data; <https://www.naturalearthdata.com/>) and prepared using QGIS version 3.44.

Supplementary References

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